

WHAT IS CLAIMED IS:

1 1. A method for determining whether a test compound modulates the drug
2 resistance of a cell, the method comprising:

3 a) determining the level of expression or activity of a resistance sequence in a cell
4 in the presence of a test compound; ✓

5 b) determining the level of expression or activity of the resistance sequence in the
6 cell in the absence of the test compound; and

7 c) identifying the compound as a modulator of drug resistance of the cell if the
8 level of expression or activity of the resistance sequence in the cell in the presence of the test
9 compound differs from the level of expression of the resistance sequence in the cell in the
10 absence of the test compound.

up or down
no use
for
"up"

1 2. The method of claim 1, wherein the resistance sequence is a nucleic acid
2 encoding a protein selected from the group consisting of semaphorin D, B94, mel-14 antigen,
3 24p3, proliferin, and maspin.

1 3. The method of claim 1, wherein the resistance sequence is a polypeptide
2 selected from the group consisting of semaphorin D, B94, mel-14 antigen, 24p3, proliferin,
3 and maspin.

1 4. The method of claim 1 wherein the resistance sequence is encoded by an
2 endogenous gene.

1 5. A method for determining whether a test cell has a drug-resistant
2 phenotype, the method comprising:

3 a) measuring the expression or activity of a resistance sequence in the test cell;
4 b) comparing the expression or activity of the resistance sequence measured in
5 step a) to the expression or activity of the resistance sequence in a control cell not having a
6 drug-resistant phenotype; and

7 c) determining that the test cell has a drug resistant phenotype if the expression or
8 activity of the resistance sequence in the test cell differs compared to the expression or
9 activity of the resistance sequence in the control cell.

1 6. The method of claim 5, wherein the resistance sequence is selected from
2 the group consisting of semaphorin D, B94, mel-14 antigen, 24p3, proliferin, and maspin.

1 7. A method for determining whether a subject has or is at risk of developing
2 a drug resistant tumor, the method comprising:

3 a) measuring the expression of an up-regulated or down-regulated resistance
4 mRNA in a biological sample comprising tumor cells obtained from the subject;
5 b) comparing the expression of the mRNA measured in step a) to the expression
6 of the mRNA in a control biological sample that is not drug resistant; and
7 c) determining that the patient has or is at risk of developing a drug resistant
8 tumor if the expression of an up-regulated mRNA in the biological sample obtained from the
9 patient is higher than the expression of the up-regulated mRNA in the control biological
10 sample, or decreased expression of a down-regulated mRNA in the biological sample
11 obtained from the patient is lower than the expression of the down-regulated mRNA in the
12 control biological sample.

1 8. A method for treating a drug resistant tumor in a patient, the method
2 comprising administering to said subject an amount of an up-regulated protein antagonist or a
3 down-regulated protein agonist effective to reduce drug resistance of said tumor in the
4 patient.

1 9. A method for determining whether a drug therapy should be continued in a
2 patient, the method comprising:

3 a. obtaining a biological sample comprising tumor cells from the patient;
4 b. determining the expression level of a resistance sequence in the patient sample;
5 c. comparing the expression level determined in step (b) with the expression of
6 the resistance sequence in a drug sensitive biological sample; and
7 d. discontinuing treatment when the expression level of the resistance sequence
8 in the patient sample is altered compared to the expression of the resistance sequence in the
9 drug sensitive sample.

1 10. The method of claim 9, wherein the resistance sequence is an up-regulated
2 sequence and treatment is discontinued when expression of the sequence is increased
3 compared to the expression of the sequence in the drug sensitive sample.

1 11. The method of claim 9, wherein the resistance sequence is a down-
2 regulated sequence and treatment is discontinued when expression of the sequence is
3 decreased compared to the expression of the sequence in the drug sensitive sample.

1 12. A method for determining whether a drug therapy should be continued in a
2 patient, the method comprising

3 a. obtaining a first patient biological sample comprising tumor cells and a second
4 biological sample comprising tumor cells, wherein the first sample is obtained prior to the
5 second sample;

6 b. determining the expression level of a resistance sequence in the second
7 sample;

8 c. determining the expression level of a resistance sequence in the first sample;

9 c. comparing the expression level of the resistance sequence determined in step
10 (b) to the expression level of the resistance sequence in step (c); and

11 d. discontinuing treatment when the expression level of the second sample differs
12 from the expression level of the resistance sequence in the first sample.

1 13. The method of claim 12, wherein the resistance sequence is an up-
2 regulated sequence and treatment is discontinued when expression of the sequence in the
3 second sample is increased compared to the expression of the sequence in the first sample.

1 14. The method of claim 12, wherein the resistance sequence is a down-
2 regulated sequence and treatment is discontinued when expression of the sequence in the
3 second sample is decreased compared to the expression of the sequence in the first sample.

1 15. A method for treating a drug resistant tumor in a patient, the method
2 comprising administering to the patient a compound that reduces the expression of a protein
3 selected from the group consisting of: semaphorin D, B94, mel-14 antigen, 24p3, and
4 proliferin.

1 16. A method for treating a drug resistant tumor in a patient, the method
2 comprising administering to the patient a compound that reduces the activity of a protein
3 selected from the group consisting of: semaphorin D, B94, mel-14 antigen, 24p3, and
4 proliferin.

1 17. A method for treating a drug resistant tumor in a patient, the method
2 comprising administering to the patient a compound that increases the expression of maspin.

1 18. A method for treating a drug resistant tumor in a patient, the method
2 comprising administering to the patient a compound that increases the activity of maspin.

1 19. A method for determining whether a drug therapy should be continued in a
2 patient, the method comprising

3 a. obtaining a first patient biological sample comprising tumor cells and a second
4 biological sample comprising tumor cells, wherein the first sample is obtained prior to the
5 second sample;

6 b. determining the expression level of a gene selected from the group consisting
7 of: semaphorin D, B94, mel-14 antigen, 24p3, and proliferin in the second sample;

8 c. determining the expression level of the selected gene in the first sample;

9 c. comparing the expression level determined in step (b) to the expression level
10 determined in step (c); and

11 d. discontinuing treatment when the expression level determined in step (b) is
12 greater than the expression level determined in step (c).

1 20. A method for determining whether a drug therapy should be continued in a
2 patient, the method comprising

3 a. obtaining a first patient biological sample comprising tumor cells and a second
4 biological sample comprising tumor cells, wherein the first sample is obtained prior to the
5 second sample;

6 b. determining the expression level of maspin in the second sample;

7 c. determining the expression level of maspin in the first sample;

8 c. comparing the expression level determined in step (b) to the expression level
9 determined in step (c); and

10 d. discontinuing treatment when the expression level determined in step (b) is
11 less than the expression level determined in step (c).

1 21. The method of claim 19 or 20 wherein the expression level is determined
2 by measuring mRNA expression.

1 22. The method of claim 19 or 20 wherein the expression level is determined
2 by measuring protein expression.

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